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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/705,300	11/10/2003	David H. Parma	NEX40CUSDC2	8392

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EXAMINER	
SHIN, DANA H	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 11/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/705,300	PARMA ET AL.	
	Examiner	Art Unit	
	Dana Shin	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *65-72* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *65-72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1-7-04, 1-28-05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

Sequence Rule Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below.

CFR §1.821(d) reads as follows:

> Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims or the patent application.

Figures 1A-1C, 12, and 15-16 of the instant application contain nucleic acid sequences which are not preceded by "SEQ ID NO:". Applicants are reminded that either the brief description of drawings for the Figures or Figures themselves should make a reference to the sequences by use of the sequence identifiers in accordance with CFR §1.821 through 1.825. Applicants are also reminded that the nucleic acid sequences depicted in Figures 1A-1C, 12, and 15-16 must be entered in the paper copy of sequence listing as well as CRF. See Notice to Comply. Any response to this action must correct this deficiency, as this requirement will not be held in abeyance.

Response to Arguments/Election

Applicant's election with traverse of SEQ ID NOs:206 and 185 in the reply filed on October 17, 2006 is acknowledged. The traversal is on the ground(s) that more than one SEQ ID NOs were examined for previous applications and that it is not burdensome to search all claimed SEQ ID NOs. This is not found persuasive because only the instant application, not related applications, is being examined on the merits in the instant case and because it would impose a serious search burden on the examiner to search all distinct inventions such as the instantly claimed multiple SEQ ID NOs. For example, each SEQ ID NO is regarded as a patentably distinct invention because the originally claimed multiple SEQ ID NOs have materially different nucleic acids of different lengths and also have different degrees of binding affinity to a given target gene as evidenced by the instant disclosure. Due to these different properties, the originally claimed SEQ ID NOs are not obvious variants nor do they overlap in scope, thus to search all claimed SEQ ID NOs would impose a serious search burden on the examiner. Of record, examiner notes that applicants have voluntarily cancelled non-elected SEQ ID NOs in their election with traverse, therefore, the examiner is compelled to examine only SEQ ID NOs:185 and 206 in the instant case.

The requirement is still deemed proper and is therefore made FINAL.

Status of Claims

Claims 65-72 are pending and SEQ ID NOs: 199-247, 251-290, 67-117, 129-196, and 293-388 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn

to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on October 17, 2006.

Accordingly, claims 65-72 pertaining to SEQ ID NOs:206 and 185 are currently under examination on the merits.

Priority

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed applications filed prior to PCT/US96/09455 (June 5, 1996) fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. It is found that none of the related applications filed prior to PCT/US96/09455 disclose the instantly elected inventions SEQ ID NOs:185 and 206.

Accordingly, the effective filing date for the instant application will be June 5, 1996. If applicants believe that applications filed prior to PCT/US96/9455 disclose the instantly claimed invention, applicants are encouraged to point out the particulars in response to this Office action.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on January 7, 2004 and January 28, 2005 has been placed in the application file and is being considered by the examiner. It is noted, however, that the non-patent literature citations do not have appropriate titles. Correction is required.

Specification

The abstract of the disclosure is objected to because it does not contain any statement to which the instantly claimed invention pertains. Note that there is no statement pertinent to a method of therapy or treatment, as claimed in the instant application. Correction is required. See MPEP § 608.01(b).

The disclosure is objected to for containing sequence rule non-compliant subject matter in Figures 1A-1C, 12, 15-16 and at least pages 40, 58, and 69 of the instant specification. See Notice to Comply. It is suggested that applicants review the entire disclosure to comply with sequence rules. Appropriate correction is required.

The disclosure is objected to because of the following informalities: On page 116, it appears that the title of the table is misspelled. See "Tabl 20" in line 1 and "Sp cificity" in line 2. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 65-72 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to a method for treating a lectin-mediated platelet disorder, inflammation or lymphocyte tracking disorder comprising administering nucleic acid ligands to P-selectin (SEQ ID NO:206) or L-selectin (SEQ ID NO:185).

The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'." (Wands, 8 USPQ2d 1404). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction

provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

As claimed, the breadth of the instant claims embraces only *in vivo* therapeutic methods. The state of the art pertinent to nucleic acid-mediated therapy, in particular with regard to aptamers as claimed in the instant case, was considerably nascent at the time the instant application was originally filed in 1996. That is, one of ordinary skill in the art would not have known how to use the aptamer-mediated therapeutic methods without proper guidelines and determine whether a particular nucleic acid sequence for an aptamer would function as a pharmaceutical agent to treat a desired disorder without appropriate *in vivo* evidence. See, for example, the review article by Stull et al. (*Pharmaceutical Research,* April, 1995, 12:465-483). With regard to aptamers, the article teaches the following on page 466:

"To date, only a few instances of oligonucleotide aptamers displaying biological effects have been reported (Table II)."

Table II of the article clearly demonstrates that by April, 1995, only one aptamer showed requisite *in vitro* and *in vivo* aptamer-mediated inhibition of gene expression. Stull et al. further note obstacles to *in vivo* application of nucleic acid drugs on page 478:

"In summary, advances in molecular biology and synthetic chemistry have led to novel nucleic acid drugs to inhibit gene expression and protein function. However, the delivery and entry of nucleic acid drugs into the target site remains a major obstacle to the successful introduction of this aspect of the molecular biology revolution into a clinical setting."

Even a decade after the filing date of the instant application, the state of the therapeutic aptamer art remains unpredictable to the extent that one of ordinary skill in the art cannot predict

the "therapeutic" effects of any aptamer selected by SELEX without undue experimentation. Consider, for example, the 2006 review article by Fichou et al. (*TRENDS in Biotechnology,* Available online October 12, 2006, volume is not yet assigned).

Fichou et al. teach challenges and limitations to be overcome with regard to therapeutic/clinical use of aptamers as following:

"The main limitation of aptamers is that local administration is required; *in vivo* systemic delivery would not be appropriate because proteins in untargeted organs could be impaired." (page 6)

"Thus far, Vitravene (antisense oligonucleotide) and Macugen (aptamer) are the sole therapeutic oligonucleotides but, although many improvements are required in delivery and *in vivo* efficiency, there is no doubt that a growing number of aptamers and, it is to be hoped, siRNAs will soon be used for the treatment of diseases." (pages 6-7)

Fichou et al. further note the unpredictable nature of nucleic acid drugs, in particular, DNA decoy oligonucleotide, on page 6:

"A recent phase III randomized, double-blind, placebo-controlled clinical trial (PREVENT IV) treated vein grafts from 1508 patients, who were undergoing CABG surgery, *ex vivo* with an E2F decoy, Edifoligide. Unfortunately, patients engrafted with veins treated with the decoy did not show beneficial effects more than 1 year after treatment when compared with those who received placebo vein grafts. This illustrates the major challenge of translating promising data in animal models into success in clinical trials..."

In view of the foregoing, it is clear that the art of nucleic acid-mediated gene therapy, such as aptamers as claimed in the instant case, requires *in vivo* clinical data in order to use the

gene therapy method without undue experimentation. That is, one of ordinary skill in the art cannot conclude *a priori* that a particular aptamer selected by the SELEX protocol will render therapeutic effects *in vivo*. If any aptamer or nucleic acid inhibitors were designed in a laboratory and used in clinical applications without undergoing proper stages of clinical or *in vivo* tests, that is without "undue experimentation", one might reasonably ask why there is only one aptamer-based therapeutic agent (Macugen) approved by the FDA to date since the discovery of aptamers in the late 1980s. As such, it is an art-recognized viewpoint that having an aptamer sequence in hands does not indeed mirror therapeutic efficacy of the aptamer sequence and that one skilled in the art cannot determine the therapeutic efficacy of the *in vitro*-selected aptamer without undue experimentation.

In order to overcome the art-recognized unpredictability of nucleic acid drugs (i.e., aptamers), the specification must provide sufficient guidelines so as to produce the claimed therapeutic effects when the instantly claimed methods are practiced by one of ordinary skill in the art. However, the instant specification does not disclose any working examples for methods of treating lectin-mediated disorders comprising administering SEQ ID NOs: 206 or 185. Moreover, the instant disclosure does not set forth any specific guidance/direction as to how to practice the instantly claimed treatment methods (i.e, method steps or protocols) or how to obtain the therapeutic effects required by the claims. For instance, one of ordinary skill in the art would not know what is embraced by the term "pharmaceutically effective amount" because there are no guidelines for determination of aptamer dosages needed to provide a therapeutic effect and there is no standard by which to measure whether the lectin aptamers will pharmaceutically operate *in vivo* as intended and claimed. The only method examples provided by the instant

specification are *in vitro* binding affinity assays: Figure 11, Examples 16 and 24 for SEQ ID NO:185 and Example 30 for SEQ ID NO:206. With regard to the instantly claimed treatment method, the specification states "because of their ability to selectively bind lectins, the nucleic acid ligands to lectins described herein are useful as pharmaceuticals. This invention, therefore, also includes a method for treating lectin-mediated diseases by administration of a nucleic acid ligand capable of binding to a lectin." See page 19, lines 7-10. The mere statement that lectin ligands would be useful for treating lecin-mediated diseases based solely on their ability to selectively bind lectins does not enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the lectin ligands for therapeutic applications in all organisms *in vivo* as broadly claimed in the instant case. Conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of treating lectin-mediated diseases comprising administering a therapeutically effective amount of a nucleic acid ligand to a lectin.

In re Vaeck, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991), the Court ruled that a rejection under 35 U.S.C. 112, first paragraph for lack of enablement was appropriate given the relatively incomplete understanding in the biotechnological field involved, and the lack of a reasonable correlation between the narrow disclosure in the specification and the broad scope of protection sought in the claims.

Further, the broadly claimed methods without reciting the specific structure of the lectin ligand (i.e., SEQ ID NOs and type of target lectin) in claims 65-67 and 69-71 encompass any nucleic acid ligand to any lectin, which is required to elicit pharmaceutical/therapeutic activity in any living organism toward any lectin.

Corollary to the instant case, in *In re Wright,* 999 F.2d 1557, 27 USPQ2d 1510 (Fed. Cir. 1993), the court affirmed the Board's decision and stated that the evidence did not show that a skilled artisan would have been able to carry out the steps required to practice the full scope of claims which encompass "any and all live, non-pathogenic vaccines, and process for making such vaccines, which elicit immunoprotective activity in any animal toward any RNA virus." 999 F.2d at 1562, 27 USPQ2d at 1513 (original emphasis).

Accordingly, in view of the totality of the factors/reasons stated above, it would require undue experimentation for one skilled in the art to practice the entire scope of the claimed invention at the time of filing, absent evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re*

Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 65-72 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2 and 4-7 of U.S. Patent No. 6,544,959 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the reasons set forth below:

The instant claims are directed to a method for treating a lectin-mediated platelet disorder (claim 65) or a lectin-mediated inflammation/lymphocyte tracking disorder (claim 69) comprising administering a nucleic acid ligand to a lectin, wherein said lectin is P-selectin (claim 67) or L-selectin (claim 71) and said nucleic acid ligand is SEQ ID NO:206 (claim 68) or SEQ ID NO:185 (claim 72).

Claim 1 of U.S. Patent No. 6,544,959 B1 broadly recites a method for treating a lectin-mediated disease comprising administering a pharmaceutically effective amount of a nucleic acid

ligand to a lectin. The specification of the U.S. Patent discloses that the term "lectin-mediated disease" encompasses a variety of leukocyte-mediated disease states including inflammation and coagulation and teaches that lectin antagonists may have therapeutic applications in treating lectin-mediated inflammation and coagulation. See column 2, lines 18-27.

Although the instantly recited "lectin-mediated platelet disorder" or "lectin-mediated inflammation" are not identical with claim 1 U.S. Patent No. 6,544,959 B1 word for word, the scope of patent protection sought by the broadly claimed method of claim 1 of U.S. 6,544,959 B1 embodies methods for treating a lectin-mediated platelet disorder and a lectin-mediated inflammation in light of the reasons stated above.

Further, the abbreviated "P" for P-selectin represents platelets, and the abbreviated "L" for L-selectin represents lymphocytes. See page 379 of Bevilacqua et al. (*Journal of Clinical Investigation,* 1993, 91:379-389). Thus, by virtue of the inherently implied nomenclature, it is *prima facie* obvious that the method claim wherein said selectin is L-selectin (claim 4, US 6,544,959 B1) or P-selectin (claim 5, US 6,544,959 B1) clearly reads on the method claim for treating a lymphocyte tracking disorder (claims 69 and 71, instant application) or a lectin-mediated platelet disorder (claims 65 and 67, instant application), respectively.

Given that the independent claims 65 and 69 are commensurate in scope with claim 1 of U.S. 6,544,959 B1, it reasonably follows that dependent claims are commensurate in scope with the respective claims of U.S. 6,544,959 B1 as indicated below:

1) Claims 66 and 70 are commensurate in scope with claim 2 of U.S. Patent No. 6,544,959 B1.

2) Claim 67 is commensurate in scope with claim 5 of U.S. Patent No. 6,544,959 B1.

3) Claim 68 is commensurate in scope with claim 7 of U.S. Patent No. 6,544,959 B1.

4) Claim 71 is commensurate in scope with claim 4 of U.S. Patent No. 6,544,959 B1.

5) Claim 72 is commensurate in scope with claim 6 of U.S. Patent No. 6,544,959 B1.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dana Shin whose telephone number is 571-272-8008. The examiner can normally be reached on Monday through Friday, from 8am-4:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Dana Shin
Examiner
Art Unit 1635

TC1600

JANE ZARA, PH.D.
PRIMARY EXAMINER

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 37 CFR §1.821(g). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. §§1.821 - 1.825 for the following reason(s):

- [X] 1. This application clearly fails to comply with the requirements of 37 C.F.R. §§1.821-1.825. Applicants attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).
- [ ] 2. This application does not contain, as a separate part of the disclosure on paper copy, a Sequence Listing as required by 37 C.F.R. §1.821(c).
- [ ] 3. A copy of the Sequence Listing in computer readable form has not been submitted as required by 37 C.F.R. §1.821(e).
- [ ] 4. A copy of the Sequence Listing in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. §1.822 and/or 1.823, as indicated on the attached copy of the marked-up Raw Sequence Listing.
- [ ] 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. §1.825(d).
- [ ] 6. The paper copy of the Sequence Listing is not the same as the computer readable from of the Sequence Listing as required by 37 C.F.R. §1.821(e).
- [ ] 7. Other:

Applicant Must Provide:

- [X] An initial or substitute computer readable form (CRF) copy of the Sequence Listing. (If the unidentified sequences are not provided on the CRF)
- [X] An initial or substitute paper copy of the Sequence Listing, as well as an amendment directing its entry into the specification. (If the unidentified sequences are not provided in the paper copy)
- [X] A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. §1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). (If a new paper and/or CRF are required)

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
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